

## Case Report: Unmasking Leprosy: An Unusual Immune Reconstitution Inflammatory Syndrome in a Patient Infected with Human Immunodeficiency Virus

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**Abstract.** Immune reconstitution inflammatory syndrome (IRIS) has become a frequent and potentially severe complication after initiation of following antiretroviral therapy (ART) in patients infected with human immunodeficiency virus (HIV). IRIS can unmask a previously clinically silent infection, such as tuberculosis, as recently described for *Mycobacterium* infections. We describe a case in a patient from Côte d'Ivoire living in France in whom skin papular lesions developed after initiation of ART. These lesions were associated with microbiologically proven leprosy. Thus, latent leprosy can appear as IRIS, and leprosy-associated IRIS should be considered in HIV-infected patients from areas endemic for leprosy.

New clinical symptoms may occur soon after introduction of antiretroviral therapy (ART) in patients infected with human immunodeficiency virus (HIV) as immune reconstitution inflammatory syndrome (IRIS).<sup>1</sup> IRIS has been initially reported as a paradoxical exacerbation of a pre-existing, treated, opportunistic infection after ART introduction in the absence of treatment failure, or as any new opportunistic infection seen as an immune response improvement.<sup>1</sup> It may also reflect emergence of a previously clinically silent infection in the course of immunologic restoration. Diagnosis of these underlying infections may constitute a challenge for the clinician. We report an HIV-infected patient from Africa living in France in whom skin lesions developed after initiation of ART. These lesions were caused by *Mycobacterium leprae*.

A 40-year-old man was admitted to the Center d'Infectiologie Necker-Pasteur in Paris, France, for recent skin lesions. A native of Côte d'Ivoire, he had been living in France since 2003, and had returned to Côte d'Ivoire in 2006 and 2007. HIV-1 infection was diagnosed in 2004 with 106 CD4<sup>+</sup> lymphocytes/mm<sup>3</sup> (5%) and an HIV RNA viral load of 5.1 log<sub>10</sub> copies/mL. The patient was treated with zidovudine/lamivudine and lopinavir/ritonavir, and then with abacavir, tenofovir, and lopinavir/ritonavir. However, he showed poor compliance with treatment, and viral load never decreased to less than 3.9 log<sub>10</sub> copies/mL. ART was stopped by the patient in April 2008.

In March 2009, analyses showed 8 CD4<sup>+</sup> lymphocytes/mm<sup>3</sup> (1%) and a viral load of 5 log<sub>10</sub> copies/mL. Treatment was then switched to lopinavir/ritonavir, tenofovir, and abacavir/lamivudine, according to viral resistance genotyping. The patient showed good compliance, and two months later the CD4<sup>+</sup> cell count increased to 117 lymphocytes/mm<sup>3</sup> (6%) and the viral load decreased to 2.4 log<sub>10</sub> copies/mL.

In May 2009, he reported progressive occurrence of several painless, infiltrated, centimetric and non-pruriginous skin lesions. Clinical examination showed 11 erythematous papules, sometimes covered with gray squamiae and located on

the forehead, ears, eyelids, right internal canthus, and upper limbs (Figure 1). No other physical abnormality was found. The C-reactive protein level was 13 mg/L. Results of standard biological analyses were normal. A few acid-fast bacilli were found on a cutaneous smear after Ziehl staining (Supplemental Figure, available at [www.ajtmh.org](http://www.ajtmh.org)). Skin biopsy specimens showed non-caseating epithelioid granulomas. Ziehl, periodic acid–Schiff, Giemsa and Grocott stainings showed negative results on skin biopsy specimens (Figure 2). Results of a chest radiograph and abdominal computed tomography were normal. Results of tests for acid-fast bacilli in sputum and analysis of gastric fluid, urine, blood, and bone marrow were negative. A specific *M. tuberculosis* complex polymerase chain reaction performed on skin biopsy specimens showed negative results.

Treatment with clarithromycin, ethambutol, and rifabutin was started because an *M. avium* complex infection was suspected. A 16S–23S ribosomal RNA-specific polymerase chain reaction and sequencing performed on skin biopsy samples identified *M. leprae*. Electromyography showed damage on the right ulnar nerve. A diagnosis of a borderline lepromatous form of leprosy was made and treatment was changed to clarithromycin, ethionamide, and dapsone. Clarithromycin was given instead of rifampin because of major interactions with ART. Skin lesions progressively cleared but became hypoesthetic. The patient is still receiving therapy, with no other complication reported as of January 2010, after six months of treatment. We plan a minimal duration of treatment of 12 months.

Although HIV has never been shown to increase susceptibility to *M. leprae*, latent leprosy infections can be unmasked as IRIS after initiation of ART.<sup>2,3</sup> The concept of silent infection becoming clinically patent upon rapid restoration of immune responses has been documented for other human pathogenic mycobacteria such as *M. tuberculosis*.<sup>4</sup> In HIV-infected patients, IRIS caused by *M. tuberculosis* is associated with an increase in the number of activated tuberculin-specific effector memory CD4<sup>+</sup> T cells and of a subpopulation of T cell antigen receptor  $\gamma\delta$  T cells.<sup>5</sup> IRIS is more frequent in naive patients with a rapid decrease of HIV viral load after ART introduction and when ART is started near the time of diagnosis of an opportunistic infection.<sup>1,6</sup> This reaction seems to be associated with an increase of T cell reactivity after ART

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FIGURE 1. Leprosy skin lesions two months after introduction of antiretroviral therapy in a human immunodeficiency virus-infected patient from Côte d'Ivoire living in France. This figure appears in color at [www.ajtmh.org](http://www.ajtmh.org).

initiation, with migration of CD4<sup>+</sup> T cells into lesions and improvement of the Th1 reaction.<sup>2</sup>

Ustianowski and others reported nine patients with ART-unmasked leprosy.<sup>2</sup> Clinical symptoms usually developed within three months after ART initiation. Such symptoms were occasionally severe and could require oral corticosteroids, along with therapy against *M. leprae*. Recent data underline the increased incidence of leprosy after initiation of ART.<sup>7</sup> However, development of papular lesions in the setting of HIV infection is evocative of other several diagnoses (*M. avium* complex infection, syphilitic nodules, histoplasmosis, disseminated cryptococcosis [umbilicated lesions], Kaposi sarcoma, leishmaniasis, and sarcoidosis). Unmasking leprosy should also be considered in HIV-infected patients from Africa beginning ART, even long after they have left disease-endemic areas. Leprosy should be promptly differentiated

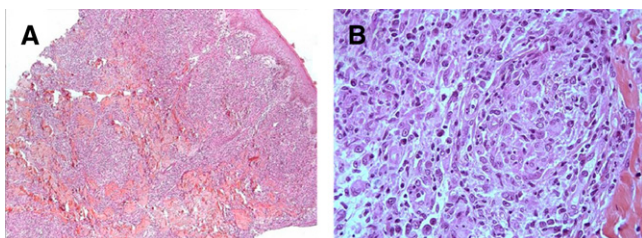


FIGURE 2. Skin biopsy specimen from the patient showing **A**, a dense infiltrate extended throughout the dermis, with collection of epithelioid cells, lymphocytes, and plasmacytes (magnification  $\times 5$ ) and **B**, non-caseating epithelioid granulomas (magnification  $\times 40$ ). (Hematoxylin and eosin stained.) This figure appears in color at [www.ajtmh.org](http://www.ajtmh.org).

from other tropical causes of IRIS such as tuberculosis, cryptococcosis, and histoplasmosis.<sup>4,8,9</sup>

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